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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,257	01/02/2000	Pierre Coutos-Thevenot	0061/00091	8211

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EXAMINER
KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
1638	15

DATE MAILED: 07/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,257	COUTOS-THEVENOT ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-29 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Sequence Rules

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth:

> § 1.821 Nucleotide and/or amino acid sequence disclosures in patent applications;
>
> (d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Applicant must amend the specification and/or drawings to insert sequence identifiers.

Specification

2. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

3. As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

> (a) TITLE OF THE INVENTION.
> (b) CROSS-REFERENCE TO RELATED APPLICATIONS.

(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.
(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is drawn towards a polynucleotide comprising a lucerne PR promoter operably linked to a stilbene synthase gene, as well as plant cell and plants comprising said polynucleotide sequence and a method of transferring plants and plant cells with said polynucleotide.

Applicant describes a nucleic acid sequence of SEQ ID NO: 3 comprising the lucerne PR1 promoter of SEQ ID NO: 1 and the stilbene synthase coding sequence of SEQ ID NO: 2.

Applicant does not describe the composition and structure of other polynucleotides comprising other Lucerne PR promoters and other stilbene synthase coding sequences.

See *University of California V. Eli Lilly and Co.,* 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

7. Claims 1-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid sequence of SEQ ID NO: 3 comprising the lucerne PR1 promoter of SEQ ID NO: 1 and the stilbene synthase coding sequence of SEQ ID NO: 2., and the transformation of ~~41B rootstock~~ apple trees therewith, does not reasonably provide enablement for the

composition and structure of other polynucleotides comprising other Lucerne PR promoters and other stilbene synthase coding sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant claims a polynucleotide sequence comprising a lucerne PR promoter inducible in plants selected from the group comprising, an IND S1 sequence, a fragment of a lucerne PR promoter having the activity of a promoter in plants, and a polynucleotide sequence that has at least 80%, 90%, or 95% sequence identity to a promoter for a lucerne PR protein; and a gene encoding a grapevine stilbene synthase selected form the group comprising *vst1* and *vst2*.

Applicant teaches isolation of PR 10 promoters by using PCR primers specific for PR proteins in lemunious plants to amplify a cDNA probe for screening a cDNA library to obtain a probe for screening an alfalfa genomic library (Example 1 page 14), expression of PR 10 promoter/GUS constructs in transformed tobacco plants (Example 2 page 24), hypersensitivity reaction test in tobacco using bacterial and fungal pathogens showing induction of PR10 promoter (Example 4 page 29). Applicant also teaches isolation of the stilbene synthase gene (*vst1*, SEQ ID NO: 2) by using data in the literature (Example 5 page 30) and by obtaining a genomic clone from BAYER AG, expression study of *vst1* gene expression in grapevine (pages 31-32 Example 5), construction of a plant PR10 promoter/stilbene synthase expression vector (page 33-34 Example 6; SEQ ID NO: 3), transformation of grapevine and activity analysis of PR10-1-*vst1*. Applicant teaches that the transgenic plants showed a 50 fold increase in the resveratrol level 9 days after biotic stress caused by *Botrytis cinerea* (page 60 in Example 7).

Applicant does not teach isolation of other PR promoters or other stilbene synthase coding sequences, nor methods of transforming plants and plant cells therewith, nor transformed plants and plant cells thereby obtained, a biotic induction of resveratrol by *Plasmora viticola,* or an abiotic induction of resveratrol by mechanical wound, insect attack, wind, frost, viral attack, in grapevine plants transformed with PR10-1-*vst1*.

The unpredictability of identifying an active promoter region from either a group comprising a large population of fragments of varying lengths or a group comprising a myriad of variations of random point mutations that have limited sequence identity to functional promoter, is illustrated in the Functional analysis of linker insertions and point mutations in the *α-Amy2/54* GA-regulated promoter (Tregear *et al.,* Plant Mol. Bio., 29: 749-758, 1995). The authors have identified, by analysis of disruptions or point mutations to the *α-Amy2/54* promoter sequence, five regions required to direct expression in aleurone protoplasts or to enhance expression (page 755, discussion, columns 1-2). It is clear that the changes made to the promoter, in some way, altered the interaction of factors that bind with these *cis* elements such that control over gene expression was lost. The loss of these *cis* elements themselves due to fragmentation of the full length promoter would either irrevocably eliminate or severely diminish the activity of the promoter.

In view of the lack of guidance as to how to isolate additional lucerne PR promoters or as to which point mutations would best serve the invention or which fragments of the lucerne PR promoter best retain activity in a plant, or what other PR promoters might show induction by *Plasmora viticola* or abiotic factors, one of skill in the art would be required to test *in planta* for induction of gene expression. Cloning the large number of constructs and making the transgenic

plants comprising those constructs to find another Lucerne promoter, or a fragment of a lucerne PR promoter having activity in plants, or a polynucleotide sequence having at least 80%, 90%, or 95% sequence identity to a promoter of a lucerne PR protein, and still able to function as an inducible lucerne PR promoter would require undue trial and error experimentation to make and use the invention.

Given the lack of guidance, the limited working examples in the specification, the breadth of the claims, and the unpredictability in the art, undue trail and error would be needed to practice the invention commensurate with the scope of the claims. Therefore, the invention is not enabled.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At Claim 1, line 1, the claim reads "Nucleic acid which comprises the sequence of the promoter", the claim should read, --An isolated nucleic acid comprising a sequence of a promoter--.

At Claim 1, line 2, the claim reads "at least the sequence of a gene encoding a stilbene synthase", is indefinite, and should read --a sequence of a gene encoding a stilbene synthase.--.

At Claim 1, line 2, "linked" should be --operably linked--.

At Claim 1, line 3, "gene" encompasses a promoter and coding DNA. It is not clear if it is Applicant's intention to claim a PR promoter linked to a stilbene synthase promoter linked to a stilbene synthase coding region or just a PR promoter linked to a stilbene synthase coding region.

At Claims 1-5, line 2, "promoter for a lucerne PR protein" does not make sense. Proteins don't have promoters.

At Claim 2, the phrase "in a tissue specific manner or not" is a meaningless limitation and should be deleted.

At Claim 3, lines 5 and 10, "IND S1 sequence" is indefinite because it is not clear what is encompassed.

At Claim 3, the claim uses improper Markush group language.

At Claim 3, part b), the claim recites "the sequence which is of a fragment of the IND S1 sequence and which has a promoter sequence effect in plants," It is recommended that Applicant amend to claim to read, --the sequence which is a fragment of the IND S1 sequence and which functions as a promoter in plants,--.

At Claims 3-5, the meaning of "homology" is unclear because it has been used to describe both the sequence and the function of biological polymers. The phrase --sequence identity-- should be substituted for homology.

At Claims 2-8, line 1, the claims read "Nucleic acid", they should read --The nucleic acid--.

At Claim 8, line 3, the claim reads "sequence selected from" it should read --sequence selected from the group consisting of--. Also, --and-- should be inserted between a) and b).

At Claim 9, line 1, the claim reads "System for expression . . .". It is unclear whether the claim is drawn to a method or product. Also, it is not known what is intended by "system". The claim should read --A plant expression vector comprising the nucleic acid of Claim 1.--. Consequently, Claim 10 should be deleted.

At Claim 11, the claim reads "Expression vector" the claim should read --The plant expression vector of Claim 9, wherein the vector is a plasmid.--.

At Claim 11-19, line 1 the claims read "Expression system" they should read --The plant expression vector--.

At Claim 19, line 2, "a physical phenomena such as" is indefinite and should be removed.

At Claim 20, line 1, the claim reads "The plant cell which is transformed with a system or vector according to Claim 9", it should read, --Plant cells transformed with the plant expression vector of Claim 9.--.

At Claim 21, line 1, the claim reads "Cell" it should read --The plant cell--.

At Claim 22, the claim reads "Process for obtaining a cell according to Claim 20, wherein a plant cell is transformed using a microbiological method including a system for expressing a stilbene synthase gene in plants comprising at least one nucleic acid." It is recommended that the claim be amended to recite, --A method for making the plant cell of Claim 20, wherein a plant cell is transformed with *Agrobacterium* comprising a plant expression vector comprising a promoter for a lucerne PR gene operably linked to a coding sequence of a stilbene sythase gene.--.

At Claim 23, the Claim reads, "Process for obtaining plants which express a stilbene synthase gene, characterized in that cells of the said plant are transformed using a system or a

vector according to Claim 9, the cells expressing the said gene are selected and a plant is regenerated from these cells.", the claim should read, --A method for obtaining plants that express stilbene synthase comprising: transforming plant cells with the plant expression vector of Claim 9, and regenerating transformed plants from said cells, wherein said plants express stilbene synthase.--.

At Claim 24, the Claim reads "Plant comprising an expression system according to Claim 9.", the Claim should read, --A transformed plant comprising the plant expression vector of Claim 9.--.

At Claim 25, the Claim reads "Plant comprising cells according to Claim 20.", the claim should read, --A transformed plant comprising the plant cell of Claim 20.--.

At Claim 26, the Claim reads, "Plant which is obtained by implementing a process according to Claim 22.", the Claim should read, --A transformed plant made by the method of Claim 23.--.

At Claim 27, the Claim reads, "Plant according to Claim 24 characterized in that it is a plant of agricultural interest.", the Claim should read, --The transformed plant of Claim 24, wherein said plant is a plant of agricultural interest.--.

At Claim 28, the Claim reads, "Plant according to Claim 27, characterized in that the plant is grapevine.", the Claim should read, --The transformed plant of Claim 27, wherein the plant is grapevine.--.

At Claim 29, the Claim reads, "Process for obtaining a cell according to Claim 21, wherein a plant cell is transformed using a microbiological method including a vector for expressing a stilbene synthase gene in plants comprising at least one nucleic acid." It is

recommended that the claim be amended to recite, --A method for making the plant cell of Claim 21, wherein a plant cell is transformed by *Agrobacterium* comprising a plant expression vector comprising a promoter for a lucerne PR gene operably linked to a coding sequence for a stilbene synthase gene.--.

10. Claims 1-29 are deemed free of the prior art, given the unpredictability inherent in the process as stated above, and the failure of the prior art to teach or reasonably suggest an isolated cDNA or genomic DNA sequence encoding stilbene synthase from grapevine linked to a lucerne PR promoter.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the legal analyst, Kim Davis, whose telephone number is (703) 308-0009.

Amy Nelson

Russell Kallis Ph.D.
July 1, 2002

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